Introduction to mrgsolve : Hands on tutorial

Kyle Baron and Ana Ruiz

Metrum Research Group and Gilead Sciences

Red Iberoamericana de Farmacometria 2022
September 28, 2022

Red Iberoamericana de Farmacometría

Presentation Overview

Components

Minimum Components

Closed-form

- $PROB
- $GLOBAL
- $PKMODEL
- $CMT
- $PARAM
- $CAPTURE

ODEs

- $PROB
- $GLOBAL
- $CMT
- $PARAM
- $ODE
- $CAPTURE

IV Models

Closed-form

```
$PROB
#one compt model (IV administration)

$GLOBAL
#define CP (CENT/V)

$PKMODEL ncmt = 1, depot = FALSE

$PARAM @annotated
CL   :  1 : Clearance (volume/time)
V    : 20 : Central volume (volume)
```

```

$CMT @annotated
CENT   : Central compartment (mass)

$CAPTURE @annotated
CP : Plasma concentration (mass/time)
```

IV Models

ODEs

```
$PROB
#one compt model (IV administration)
$GLOBAL
#define CP (CENT/V)

$CMT  @annotated
CENT : Central compartment

$PARAM @annotated
CL   :  1 : Clearance (volume/time)
V    : 20 : Central volume (volume)
```

```

$ODE
dxdt_CENT =  - CL*CP;

$CAPTURE @annotated
CP : Plasma concentration (mass/volume)


```

Absorption Models

Closed-form

```
$PROB
#one compt model with first order absorption

$GLOBAL
#define CP (CENT/V)

$PKMODEL ncmt = 1, depot = TRUE

$CMT  @annotated
EV   : Extravascular compartment
CENT : Central compartment
```

```
$PARAM @annotated
CL   :  1 : Clearance (volume/time)
V    : 20 : Central volume (volume)
KA   :  1 : Absorption rate constant (1/time)

$CAPTURE @annotated
CP : Plasma concentration (mass/volume)
```

Absorption Models

ODEs

```
$PROB
#one compt model with
    first order absorption
$GLOBAL
#define CP (CENT/V)

$CMT  @annotated
EV   : Extravascular
    compartment
CENT : Central compartment


$PARAM @annotated
CL   :  1 : Clearance (
    volume/time)
V    : 20 : Central volume
     (volume)
KA   :  1 : Absorption
    rate constant (1/time)
```

```


$ODE
dxdt_EV = -KA*EV;
dxdt_CENT = KA*EV  - CL*CP
    ;

$CAPTURE @annotated
CP : Plasma concentration
    (mass/volume)


```

Covariates

Covariates

- Covariates must be defined under $MAIN and $PARAM

```
[PARAM] @annotated
WT    : 70 : Weight (kg)
CLCR  : 83 : Creatinine
    clearance (ml/min)
AGE   : 35 : Age (years)

[MAIN]

double TVCL      = THETA1;
double CL_AGE    = THETA5;
double CL_CLCR   = THETA9;
```

```

double LOGTWT = 0.75*log((
    WT/70.0));
double LOGTAGE = log((AGE/
    35.0));
double LOGTCLCR = log((
    CLCR/83.0));
double CL =  exp(log(TVCL)
     + CL_AGE * LOGTAGE +
    CL_CLCR * LOGTCLCR +
    LOGTWT + ETA(1)) ;
```

A Case Example

BE.R

- Calculate NCA param using PKNCA library
- Forest plots with pmForest
- Use lme library for BE calculation

To do

- Build the mrgsolve model for 2 cmpt with first order absorption
- simulate salt QD vs base TID
- calculate AUC over 24 hrs